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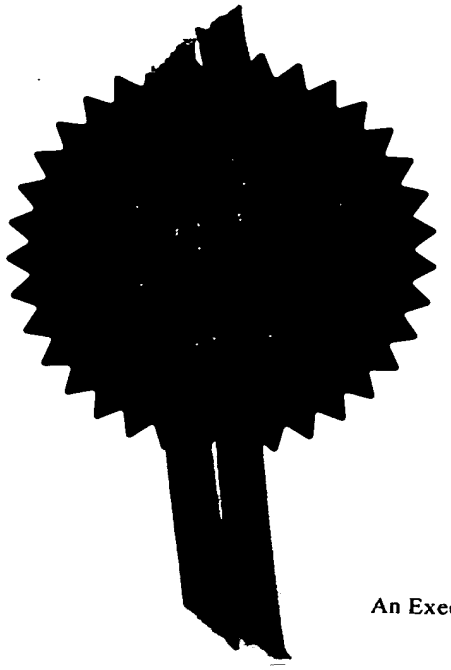

Signed Andrew Gregg

Dated 14 February 2000

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41105/JMD

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PEPTIDE THERAPEUTICS LIMITED

Peterhouse Technology Park,
100, Fulbourn Road,
Cambridge CB1 9PT.

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of incorporation

United Kingdom

0042800700 3

4. Title of the invention

Novel Peptides

5. Full name, address and postcode in the United Kingdom to which all correspondence relating to this form and translation should be sent

Reddie & Grose
16 Theobalds Road
LONDON
WC1X 8PL

Patents ADP number *(if you know it)*

91001

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Country	Priority application *(If you know it)*	Date of filing *(day/month/year)*

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Number of earlier application	Date of filing *(day/month/year)*

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Signature: Reddie & Grose

Date: 6 August 1999

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Novel Peptides

The present invention relates to novel peptide sequences, analogues, fragments thereof or mimetics of the sequences and their use in the preparation of medicaments for the treatment or prophylaxis of IgE-mediated allergies. In particular, the novel peptides are derived from regions of IgE for both passive and active immunoprophylaxis or immunotherapy. The invention further relates to methods for their production, pharmaceutical compositions containing them and their use in medicine.

The role of IgE in the mediation of allergic responses, such as asthma, food allergies, atopic dermatitis, type-I hypersensitivity and allergic rhinitis, is well known. On encountering an antigen, such as pollen or dust mite allergens, B-cells commence the synthesis of allergen specific IgE. The allergen specific IgE then binds to its high affinity receptor, FcεRI, on basophils and mast cells. Any subsequent encounter with the specific allergen has the effect of cross-linking the receptor which triggers the release of histamine and other allergic mediators from the mast cells and/or basophils. This process is known as degranulation.

A number of passive or active immunotherapeutic and immunoprophylactic approaches which interfere with this IgE-mediated histamine release mechanism have been investigated. These approaches range from the prevention of allergen/IgE complexes binding to IgE receptors on mast cells with passively administered antibodies, to competitive binding of IgE to the receptors by IgE derived peptides, to the use of specific IgE peptides for

active immunisation to elicit a protective response against IgE mediated degranulation of target cells.

There are a number of considerations, and problems, which have been encountered in the art, which have to be taken into account when designing new anti-allergy therapies. One such problem is that many known anti-IgE antibodies are anaphylactogenic, i.e. they cause triggering of basophils or mast cells by cross-linking of IgE bound to FcεRI, resulting in degranulation and release of allergic mediators. Consequently, such antibodies are therapeutically useless and indeed are likely to be positively dangerous if administered to a patient. Whether or not an antibody is anaphylactogenic, is crucially determined by the location of the target epitope on the IgE molecule.

Nonetheless, such antibodies are commercially available and have been sold as IgE detection agents for use in techniques such as Western blotting and immunohistochemistry. Those skilled in the art fully understand that in this field the mere existence of anti-IgE activity in an antibody does not imply any useful therapeutic or prophylactic properties.

Much work has been carried out by those skilled in the art to identify specific anti-IgE antibodies which do have some beneficial effects against IgE-mediated allergic reaction (WO 90/15878, WO 89/04834, WO 93/05810). Attempts have also been made to identify epitopes recognised by useful antibodies, to create peptide mimetics of such epitopes and to use those as immunogens to produce anti-IgE antibodies. Based on the present state of knowledge in this area, and despite

enormous scientific interest and endeavour, there is little or no predictability of what characteristics any antibody or epitope may have and whether or not it might have a positive or negative clinical effect on a patient.

In order to be safe and effective, the passively administered, or vaccine-induced antibodies must bind to a region which is capable of interfering with the degranulation triggering pathway without being anaphylactic *per se*. The present invention achieves these aims and provides peptides which are capable of raising non-anaphylactic antibodies which inhibit mediator release. These peptides may form the basis of an active vaccine or be used to raise appropriate antibodies for passive immunotherapy.

EP 0 477 231 B1 describes immunogens derived from the Cε4 domain of IgE (residues 497-506, also known as the Stanworth decapeptide), conjugated to Keyhole Limpet Haemocyanin (KLH) used in active vaccination immunoprophylaxis. WO 96/14333 is a continuation of the work described in EP 0 477 231 B1.

Other approaches are based on the identification of peptides which themselves compete for IgE binding to its receptors on basophils or mast cells (WO 93/04173, WO 93/04173, WO 98/24808, EP 0 303 625 B1, EP 0 341 290). Additional IgE peptides conjugated to carrier molecules are described in WO 97/31948. These immunogens may be used in vaccination studies and are said to be capable of generating antibodies that subsequently inhibit histamine release *in vivo*.

The present invention is the identification of novel segments of IgE which are used in active or passive immunoprophylaxis or therapy. These sequences have not previously been associated with anti-allergy treatments.

The peptides of the present invention are continuous sequences of IgE which have been identified as being surface exposed. They are, therefore, available for antibody recognition by auto anti-IgE antibodies. The peptides of the present invention are capable of being used in active vaccination studies to induce auto anti-IgE antibodies.

Surprisingly, the auto anti-IgE antibodies induced by the peptides of the present invention are non-anaphylactogenic and are capable of blocking IgE-mediated histamine release from target cells.

The present invention identifies those regions of IgE which are both continuous and solvent exposed. The peptides themselves may be passively administered to prevent histamine release, or may be administered in active prophylactic or therapeutic vaccination. Antibodies thus produced are active in preventing the allergic symptoms caused by triggering of target cells.

Additionally, antibodies induced in one animal may be purified and passively administered to another animal for the prophylaxis or therapy of allergy. The peptides of the present invention may also be used for the generation of monoclonal antibody hybridomas (using known techniques e.g. Köhler and Milstein, Nature, 1975, 256, p495), humanised monoclonal antibodies or CDR grafted monoclonals, by techniques known in the art. Such

antibodies may be used in passive immunoprophylaxis or immunotherapy, or used to identify IgE peptide mimetopes.

Peptides of the present invention are selected from the list comprising of;

LEDGQVMDVD	- Seq ID No. 1
TTQEGE	- Seq ID No. 2
SQKHWLSDRT	- Seq ID No. 3
TYQGHTFEDSTKKCADSNPRGV	- Seq ID No. 4

The present invention arises from the identification of these novel regions of IgE for use in allergy therapy. Therefore, the present invention includes the native IgE peptides themselves other than the known full length IgE, N and/or C terminal extension of the peptide with two residues of the natural sequences at either or both ends, and any mimetope thereof. Thus for example with Seq ID No 1, this sequence in any other sequence providing it is not the full length sequence of IgE, or for example having one of the natural residues at each end such that the sequence is LEDGQVMDVDL or WLEDGQVMDVDLS.

A mimetope can be defined as an entity that mimics the native epitope of an antibody sufficiently to be recognised by that antibody. Likewise, it may also be defined as an entity that can induce an antibody response cross-reactive to the native epitope.

More precisely a mimetope is defined as a peptide sequence which is sufficiently similar to the native IgE peptide (in sequence and/or structure) which is capable of being recognised by antibodies which recognise the native IgE peptide; or are capable of raising antibodies, when coupled to a suitable carrier, that are capable of recognising the native IgE peptide.

Those skilled in the art will realise that such polypeptides could be replaced by/modified to produce a wholly or partly non-peptide mimetic thereof; or N- and/or C-terminal derivative thereof; or an analogue thereof by virtue of amino acid deletion, addition or substitution; or a peptidomimetic thereof. In addition, these may be cyclised by techniques known in the art. Furthermore, the peptides may be modified for the purposes of ease of conjugation to a protein carrier. For example, it may be desirable for some chemical conjugation methods to include a terminal cysteine residue. In addition it may be desirable for peptides conjugated to a protein carrier to include a hydrophobic terminus distal from the conjugated terminus of the peptide, such that the free unconjugated end of the peptide remains associated with the surface of the carrier protein. Such modifications would reduce the conformational degrees of freedom of the peptide, thereby increasing the probability that the peptide is presented in a conformation that most closely resembles that of the IgE peptide *in situ*, I.e. in the native IgE molecule. For example, the peptides may be altered to have an N-terminal cysteine and a C-terminal hydrophobic and amidated tail. Alternatively, the addition or substitution of a D-stereoisomer of one or more of the amino acid residues may be performed to create a beneficial derivative, for example to enhance stability of the peptide.

Further those skilled in the art will realise that sequences can comprise these disclosed sequences. Alternatively, sequences will be consist of these sequences will the addition or not of N and/or C terminal

extensions of one or two of the natural residues at one or both ends. Further sequences will comprise these sequences of no more than 25 residues, preferably 20, more preferably 15, most preferably 9. Further the sequences will have a minimum length of 20, preferably 15 more preferably 7,most preferably 5.

Alternatively, peptide mimetopes may be identified using antibodies which are capable themselves of binding to the IgE peptides of the present invention using techniques such as phage display technology (EP 0 552 267 B1).

In view of the foregoing description it will now be clear to those skilled in the art that the above-mentioned epitopes and polypeptides could provide a useful therapeutic/prophylactic agent. This agent could be administered (e.g. as a vaccination) by routine, clinically acceptable means in appropriate dosage forms and dosage regimes to provide patients with relief from, or protection against the adverse clinical effects and symptoms of immune reaction to allergen, e.g. in treatment/prophylaxis of allergy.

Similarly, epitopes from the IgE molecule or mimetopes thereof may also be used in an active vaccination approach to the treatment of allergy.

Those skilled in the art will recognise that the epitopes, polypeptides or mimetics of the invention can be used to elicit an immune response in a host animal when conjugated to a suitable immunogenic carrier. Such suitable immunogenic carriers include albumins of sera, globulins of sera, thyroglobulins of animals, haemoglobins of animals, haemocyanins of animals,

proteins of ascaris, polylysine, polyglutamic acid, lysine-glutamic acid copolymers. In addition other suitable carriers include those such as diphtheria toxoid, tetanus toxoid and the like.

The covalent coupling of the peptide to the immunogenic carrier can be carried out in a manner well known in the art. Thus, for example, for direct covalent coupling it is possible to utilise a carbodiimide, glutaraldehyde or (N-[γ-maleimidobutyryloxy] succinimide ester. After the coupling reaction, the immunogen can easily be isolated and purified by means of a dialysis method, a gel filtration method, a fractionation method etc.

Administration without or with an adjuvant is also envisaged, such as mixing with aluminium hydroxide.

The immunogens of the present invention may comprise the peptides as previously described, including mimetopes or analogues thereof, or may be immunologically cross-reactive derivatives or fragments thereof. Also forming part of the present invention are portions of nucleic acid which encode the immunogens of the present invention or peptides, mimetopes or derivatives thereof.

Peptides used in the present invention can be readily synthesised by solid phase procedures well known in the art. Suitable syntheses may be performed by utilising "T-boc" or "F-moc" procedures.

Cyclic peptides can be synthesised by the solid phase procedure employing the well-known "F-moc" procedure and polyamide resin in the fully automated apparatus.

Alternatively, those skilled in the art will know the necessary laboratory procedures to perform the process manually.

The present invention, therefore, provides novel peptides for use in the manufacture of pharmaceutical compositions for the prophylaxis or therapy of allergies. Immunogens comprising the peptides and carrier molecules are also provided for use in vaccines for the immunoprophylaxis or therapy of allergies. Accordingly, peptides or immunogens of the present invention are used in medicine, and in the medical treatment or prophylaxis of allergic disease.

IgE peptides and immunogens of the present invention may be incorporated into vaccines for the immunoprophylaxis or therapy of allergies. Therefore, vaccines of the present invention may advantageously also include an adjuvant. Suitable adjuvants for vaccines of the present invention comprise those adjuvants that are capable of enhancing the antibody responses against the IgE peptide immunogen.

The vaccines of the present invention will be generally administered for both priming and boosting doses. It is expected that the boosting doses will be adequately spaced, or preferably given yearly or at such times where the levels of circulating antibody fall below a desired level. Boosting doses may consist of the peptide in the absence of the original carrier molecule. Such booster constructs may comprise an alternative carrier or may be in the absence of any carrier.

In a further aspect of the present invention there is provided a vaccine as herein described for use in medicine.

The vaccine preparation of the present invention may be used to protect or treat a mammal susceptible to, or suffering from allergies, by means of administering said vaccine via systemic or mucosal route. These administrations may include injection via the intramuscular, intraperitoneal, intradermal or subcutaneous routes; or via mucosal administration to the oral/alimentary, respiratory, genitourinary tracts.

The amount of protein in each vaccine dose is selected as an amount which induces an immunoprotective response without significant, adverse side effects in typical vaccines. This amount will vary depending upon which specific immunogen is employed and how it is presented. Generally, it is expected that each dose will comprise 1-1000µg of protein, preferably 1-500µg, preferably 1-100µg, of which 1 to 50µg is the most preferable range. An optimal amount for a particular vaccine can be ascertained by standard studies involving observation of appropriate immune responses in subjects. Following an initial vaccination, subjects may receive one or several booster immunisations adequately spaced.

In a related aspect of the present invention are ligands capable of binding to the peptides of the present invention. An example of such ligands are antibodies (or fragments of antibodies), where said ligands are not IgE receptors. Also provided are the use of the ligands in medicine, and in the manufacture of medicaments for the treatment of allergies.

Also forming part of the present invention is a method for identifying peptide immunogens for the immunoprophylaxis or therapy of allergy by using a computer model of the structure of IgE. Analyses of the structural model enables identification of those peptides of IgE that are surface-exposed. These regions may then be formulated into immunogens and used in medicine.

The present invention is illustrated by, but not limited to the following examples.

Examples

1.1 Peptide identification

The peptides were identified by the following technique.

The modelled structure of human IgE has been described Helm (Helm, B., A. *et al* 1990. 2IgE model structure. Deposited 2nd October 1990 with PDB). Peptides were identified which were both continuous and solvent exposed. This was achieved by using Molecular Simulations software (MSI) to calculate the accessible surface area (ASA) accessibility of each IgE amino acid residues. The ASA was averaged over a sliding window of five residues, thereby identifying regions of the IgE peptides which had an average over that 5-mer of greater than 80 Å.

This test showed the following peptides to be surface exposed:

LEDGQVMDVD	- Seq ID No. 1
TTQEGE	- Seq ID No. 2
SQKHWLSDRT	- Seq ID No. 3

TYQGHTFEDSTKKCADSNPRGV - Seq ID No. 4

1.2 Synthesis of IgE peptide conjugates

The coupling reagent is a selective heterobifunctional cross-linker, one end of the compound activating an amino group of a suitable protein carrier (selected from the list above) by a succinimidyl ester and the other end coupling a sulfhydryl group of the peptide by a maleimido group. The reaction protocol is as the following:

a. Activation of the protein carrier by reaction between lysine and succinimidyl ester.
b. Coupling between activated protein carrier and the peptide cysteine by reaction with the maleimido group.

1.3 Preparation of IgE peptide-carrier conjugate

The protein carrier is dissolved in phosphate buffered saline, pH 7.2 at a concentration of 2.5mg/ml. The coupling reagent (N-[γ-maleimidobutyryloxy] succinimide ester -GMBS) is dissolved at 102.5mg/ml in DMSO and added to the protein solution. 1.025 mg of GMBS is used for 1 mg of protein carrier. The reaction solution is incubated for 1 hour (hr) at room temperature. The by-products are removed by a desalting step using a sephacryl 200HR permeation gel. The eluant used is phosphate buffered saline/ 0.01% Tween-80™, pH 6.8. The activated protein is collected and pooled. The peptide is dissolved at 4mg/ml in 0.1M acetic acid to avoid disulphide bond formation. A molar ratio of between 2 to 20 peptides per 1 activated protein carrier is used for the coupling. The peptide solution is slowly added to the protein and the mixture

is incubated for 1hr at 25°C. The pH is maintained at a value of 6.6 during the coupling phase. A quenching step is performed by addition of a solution of cysteine (4 mg/ml in 0.1M acetic acid) for 30 minutes at 25°C, and maintaining a pH of 6.5, (0.1mg of cysteine per mg activated protein carrier is required for quenching). Two dialyses against 150mM NaCl/ 0.01% Tween-80™ are performed to remove excess of cysteine and peptide.

The quenched reaction solution is sterilised by filtration through a 0.22μm membrane. The final product is a clear filterable solution conserved at 4°C. The final ratio of peptide to carrier may be determined by amino acid analysis.

1.4 ELISA assay to determine anti-antigen antibody responses

The anti-peptide and anti-carrier immune responses were investigated using an ELISA technique outlined below.

1. Microtiter plates (Nunc) were coated with the specific antigen in PBS at 4°C overnight using either (a) 2μg/ml Streptavidin (followed by incubation with 1μM biotinylated peptide for 1 hour at 37°C), or (b) protein carrier to enable detection of anti-peptide antibodies.
2. The plates were washed with three changes of 0.01% PBS-Tween-20™.
3. The plates were then "blocked" with 1% PBS-BSA/ 0.01%Tween-20™ (blocking buffer) for 1 hr at 37°C.
4. The primary antibody was added and incubated 1 hr 30 minutes at 37°C.

5. The plate was washed three times as in 2.
6. The secondary anti-mouse Ig antibody (or anti-mouse isotype specific monoclonal antibody) coupled to HRP was added and incubated for 1 hr at 37°C.
7. The plate was washed five times.
8. The plate was developed with OPD (BioRad) for 10 minutes at room temperature in the dark.
9. The reaction was stopped with 0.4N H_2SO_4.

A monoclonal anti-human decapeptide antibody (Dec7B) was used as a reference in this ELISA. This makes it possible to calculate anti-decapeptide antibody responses either in µg specific antibody per 1ml of serum (µg/ml), or as a midpoint titre. Anti-protein carrier responses were calculated as midpoint titers.

Example 2, Immunisation of mice with novel IgE peptide conjugates (peptide-BSA, peptide-BSA) induces production of anti-human IgE antibodies.

Mice were immunised with 25µg of conjugate adsorbed onto aluminium or calcium hydroxide adjuvants. They were boosted on day 21 and on day 42 and the sera collected on day 42 and 56.

Anti-human IgE response were analysed by ELISA as described below:

1. Microtiter plates (Nunc) were coated with 50µl of 2µg/ml chimaeric anti-NP human IgE (Serotec) in PBS at 4°C overnight.

2. The plates were washed three times with 0.01% PBS-Tween-20™
3. The plates were blocked with 100µl 1% PBS-BSA/0.01% Tween-20™ (Blocking Buffer) for 1 hr at 37°C.
4. The primary antibody was added and incubated for 1 and a half hr at 37°C.
5. The plates were washed three times as in step 2.
6. The secondary anti-mouse Ig antibody (or anti-mouse isotype specific monoclonal antibody) coupled to HRP was added and incubated for 1 hr at 37°C.
7. The plates were washed five times.
8. The plates were developed with 50µl OPD (BioRad) for 10 minutes at room temperature in the dark.
9. The reaction was stopped with 50µl 0.4N H_2SO_4.

Example 3, Ant-IgE induced in mice after immunisation with conjugate are non anaphylactogenic

Several dilutions of complete sera or IgG purified from conjugate immunised mice were tested in presence of basophils from freshly collected peripheral blood from allergic patients.

The anaphylactogenicity was evaluated by measuring the amount of histamine release induced by the test antibodies as detailed below.

Materials

Material	**Source (Product Code)**

Human blood	In-house from allergic donor with defined sensitivity to *Lol p* I
EDTA	BDH (100935V)
Ficoll-Paque	Pharmacia (17-0840-02)
HEPES buffered Hanks' balanced salt solution (HBH)	In-house (prepared according to Document No. srgt23
Human serum albumin (HSA)	Sigma (A8763)
Lol p I soluble extract	ALK UK (223204)
Immunotech histamine EIA kit	Serotec (2562)

Equipment	**Supplier (Code)**
50 ml plastic disposable syringes	Becton Dickinson
19 or 21 gauge sterile hypodermic needles	Becton Dickinson
Blood collection tubes	Not critical
96-well V-bottom cell culture plates	Costar (3894)
Benchtop centrifuge capable of accepting 50ml tubes, and giving 500Xg	Not critical
MRX ELISA plate reader	Dynex Technologies

Method

Blood collection and cell preparation.

Blood was collected by venepuncture into tubes containing 0.1 volumes 2.7% EDTA, pH 7.0. It was then diluted with an equal volume of HBH containing 0.1% HSA (HBH/HSA).

The resulting cell suspension was carefully layered over 50% volume Ficoll-Paque and centrifuged at 400g for 30 minutes at room temperature. The peripheral blood mononuclear cell (PBMC) layer at the interface was collected and the pellet discarded.

The cells were washed once in HBH/HSA, counted, and re-suspended in HBH/HSA at a cell density of 2.0×10^6 per ml.

Cell Incubations

100µl cell suspension was added to wells of a V-bottom 96-well plate containing 100µl diluted test sample. Each test sample was tested at a range of dilutions with 6 wells for each dilution.

Well contents were mixed briefly using a plate shaker, before incubation at 37°C for 30 minutes with shaking at 120 rpm.

For each serum dilution, 3 wells were triggered by addition of 10µl *Lol p* I extract (concentration of *Lol p* I extract not given by suppliers; final dilution 1/10000) for assessment of anaphylactogenicity and 3 wells had 10µl HBH/HSA added as control blanks. Control wells without test sample containing cells in presence or absence of *Lol p* I were routinely included to determine triggered and spontaneous release respectively. Also wells containing cells + 0.5% Igepal™ detergent were included to determine total cell histamine release.

Well contents were again mixed briefly using a plate shaker, before incubation at 37°C for a further 30 minutes with shaking at 120 rpm.

Incubations were terminated by centrifugation at 500g for 5 min. Supernatants were removed for histamine assay using the standard histamine method provided with the kit.

Treatment of Results

Anaphylactogenesis assay

Histamine release due to test samples =

% histamine release from test sample treated cells - % spontaneous histamine release.

Blocking assay

The degree of inhibition of antigen triggered histamine release was calculated using the formula:

$$\% \text{ inhibition} = 1 - \frac{\text{(histamine release from test sample treated cells*)}}{\text{(histamine release from antigen stimulated cells*)}} \times 100$$

* Values corrected for spontaneous release.

Example 4, Anti-IgE induced in mice after immunisation with conjugate are capable of blocking IgE mediated histamine release induced by allergen triggering of basophil from allergic patient.

Histamine release was measured in basophil samples triggered with various concentrations of allergen in presence or absence of several dilutions of complete sera or IgG purified from conjugate immunised mice.

Blocking activity of anti-IgE antibodies was evaluated by the measuring inhibition of histamine release induced by the allergen.

Histamine was measured as described in example 3.

Example 5, Anti-IgE induced in mice after immunisation with conjugate are capable of blocking local allergic response in the Monkey Cutaneous Anaphylaxis model.

Purified anti-IgE antibodies from mice immunised according Example 2 were inoculated intradermally into

the skin of a monkey sensitised with IgE. Blocking activity of anti-IgE antibodies was evaluated by measuring the inhibition of the local inflammation induced by the triggering of the IgE by the antigen.

Claims

1. A polypeptide which includes or consisting of a sequence of residues selected from the group consisting of

LEDGQVMDVD	- Seq ID No. 1
TTQEGE	- Seq ID No. 2
SQKHWLSDRT	- Seq ID No. 3
TYQGHTFEDSTKKCADSNPRGV	- Seq ID No. 4

2. A compound which is a wholly or partially non-peptide mimetic; or N- and/or C-terminal derivative; or analogue by virtue of conservative amino acid residue deletion, addition or substitution; or peptidomimetic of a polypeptide according to claim 1.

3. A composition which consists of a polypeptide according to claim 1 or a compound according to claim 2 together with an immunogenic carrier and an adjuvant.

4. An anti-allergy vaccine containing or consisting of a composition according to claim 3.

5. Use of a polypeptide according to claim 1 or a compound according to the claim 2 in the manufacture of a medicament for treatment/prophylaxis of an IgE-mediated immune response such as allergy.

6. A method of treatment/prophylaxis of immune response such as allergy, which comprises administering to a patient an anti-allergy effective amount of a composition according to claim 3.

7. A method of treatment/prophylaxis of immune response such as allergy, which comprises administering to a patient an anti-allergy-effective amount of a vaccine according to claim 4.

8. An anti-IgE antibody induced by a vaccine as claimed in Claim 4

9. A pharmaceutical composition for therapeutic/prophylactic treatment of IgE-mediated immune response such as allergy, comprising (A) an anti-IgE antibody together with (B) a pharmaceutically and physiologically acceptable carrier, diluent, excipient, adjuvant or the like.

10. An anti-allergy vaccine containing or consisting of a composition according to claim 9.

11. Use of an antibody as defined in Claim 9(A) in the manufacture of a medicament for treatment/prophylaxis of an IgE-mediated immune response such as allergy.

12. A method of treatment/prophylaxis of immune response such as allergy, which comprises administering to a patient an anti-allergy-effective amount of a composition according to claim 9.

13. A method of treatment/prophylaxis of immune response such as allergy, which comprises administering to a patient an anti-allergy-effective amount of a vaccine according to claim 10.

14. An anti-IgE antibody which recognises the polypeptides of claim 1 or compounds of claim 2.